

Applicants :	Bahir & Ben-Sasson	Atty. Dkt. No.	:	1120-PCT-US	
USSN	:	10/550,870	Art Unit	:	1638
Filed	:	07/24/2006	Date of office action	:	10/16/2008
Examiner	:	Li Zheng	Date of response	:	02/17/2009
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### **Remarks**

#### **Claim Status**

Claims 49-68 are pending. To expedite the prosecution of the present application, claims 60 and 68 have been amended, and claims 49-59 have been canceled without prejudice to applicants' rights to pursue the canceled subject matter in a subsequent patent application, and claim 69 is newly added. Claim 69 is the same as canceled claim 56. Accordingly, applicants submit that there is no issue of new matters and respectfully request the Examiner to enter the Amendment.

Upon entry, claims 60-69 are pending and under examination in this application.

#### **New Matter**

The Examiner contends that the limitation of "a monotonous repeat of two to six nucleotides" constitutes new matter. Applicants respectfully disagree. Applicants submit that amended claim 60 recites a "MS-like DNA fragments comprising a monotonous repeat of two to six nucleotides, wherein the DNA fragment has a length of about 70 to about 120 nucleotides long." Support for this limitation can be found, *inter alia*, on page 7, second paragraph:

In another embodiment, the MS sequence utilized in the method of the invention comprises a monotonous repeat of one to six nucleotides, at least twelve nucleotides long, with maximum length of 10,000 nucleotides. In general, the repeat will be between about 70 and 120 nucleotides long, preferably between about 80 and 110 nucleotides, more preferably between 90 and 100 nucleotides long.

Accordingly, Applicants submit that no new matter has been added.

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**Rejection Under 35 U.S.C. §112, Written Description**

Claims 49, 52-60 and 63-68 are rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. The Examiner contends that "Applicants fail to describe a representative number of the claimed MS-like sequences encompassing monotonous repeats of two to six nucleotides. For example, there could be over four thousand of possible variants for a six nucleotide sequence ...". Applicants respectfully traverse the rejection.

Applicants submit that in contrast to the Examiner's assertion of thousands of permutations, the prior art teaches that there are only a limited number of possible repeat sequences:

Taking into account that there are only 4 nucleotides present in DNA, circular permutation of repeat sequences, as well as strand complementarity, there are 6 dinucleotide, 12 trinucleotide, 39 tetranucleotide, 109 pentanucleotide, and 366 possible hexanucleotide repeat probes. (US Patent 5,679,513, column 11, line 37-42)

Applicants submit that among the 6 possible dinucleotide repeat sequences, the present specification has disclosed three (i.e. AT, AG and CT). Among the 12 possible trinucleotide repeat sequences, the present specification has disclosed four (i.e. AAG, CGG, CTG, and TTC). Among the 39 possible tetranucleotide repeat sequences, the present specification has disclosed three (i.e. ATCG, AAAT, and TTTA). The present specification also discloses one hexanucleotide repeat (see e.g. page 7, third paragraph). Taken together, Applicants submit that the present specification has provided description for a representative number of the claimed MS-like sequences encompassing monotonous repeats of two to six nucleotides.

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In view of the above remarks, Applicants respectfully request that the rejection of claims 60 and 63-68 under 35 U.S.C. §112, first paragraph, be withdrawn.

**Rejection Under 35 U.S.C. §112, Enablement**

Claims 49, 51-61 and 63-68 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner contends that the specification, while being enabling for a method of generating genetically diverse plants via the incorporation of one of the exogenous microsatellite sequences of SEQ ID NOs.1-5, does not reasonably provide enablement for a method of generating genetically diverse plants via the incorporation of any exogenous microsatellite sequences. The rejection is respectfully traversed.

Claim 60 is drawn to a method comprising the use of "MS-like DNA fragments comprising a monotonous repeat of two to six nucleotides, wherein the DNA fragment has a length of about 70 to about 120 nucleotides long" (see page 7, 2<sup>nd</sup> to 4<sup>th</sup> paragraphs). The present specification has presented clear support to the use of monotonous repeats as claimed herein (see Figures 2-7). As examples, a sequence of 2 nucleotide-repeat (SEQ ID NO.4) was used to generate the plants shown in Figures 5 and 6; two sequences of 3 nucleotide-repeat (SEQ ID NOs.2 and 5) were used to generate the plants shown in Figures 3 and 7; a sequence of 4 nucleotide-repeat (SEQ ID NO.3) was used to generate the plants shown in Figure 4; and a sequence of 6 nucleotide-repeat (SEQ ID NO.1) was used to generate the plants shown in Figure 2.

As discussed above, the prior art teaches that there are only a limited number of possible repeat sequences, namely there are 6 dinucleotide, 12 trinucleotide, 39 tetranucleotide, 109 pentanucleotide, and 366 possible hexanucleotide repeat

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sequences. In view of the level of skill in the art, one of ordinary skill in the art would readily construct a DNA fragment comprising a monotonous repeat of two to six nucleotides, and apply such DNA fragment to the method claimed herein without undue experimentation.

Applicants submit that the present application intends to provide a concept, said concept being that phenotypic variety may be generated through the insertion of micro-satellite (MS)-like sequences. The results obtained were in fact surprising, and the invention is a proof of said concept. The number of MS-like sequences should be taken globally, i.e., five MS-like sequences displayed the same result, said result being the generation of phenotypic variability. In view of the disclosure herein and the level of skill in the art, Applicants submit that one of ordinary skill in the art could readily practice the invention of claim 60 without undue experimentation.

In view of the above remarks, Applicants respectfully request that the rejection of claims 60, 61 and 63-68 under 35 U.S.C. §112, first paragraph, be withdrawn.

#### **Rejection Under 35 U.S.C. §102**

Claims 49 and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by Havukkala et al. (U.S. Patent Application Publication No. 2003/0018185). The rejection is moot because claims 49 and 59 have been canceled.

#### **Rejection Under 35 U.S.C. §103(a)**

Claims 49, 51-61 and 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Havukkala et al. (U.S. Patent Application Publication No. 2003/0018185) in view of Gallardo

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et al. (Planta 210:19-26 (1999)). The rejection is respectfully traversed.

Havukkala et al. disclose microsatellite sequences (together with flanking sequences), and methods for their use in the detection of polymorphism. The examples of Havukkala et al. refer to (1) isolation and characterization of cDNA sequences from Eucalyptus and Pinus; and 2) PCR amplification and polymorphism analysis of Pinus DNA for detecting genetic variation.

Gallardo et al. teach the expression of a conifer glutamine synthetase (GS) gene in transgenic poplar in order to improve nitrogen utilization efficiency in trees, wherein said transgenic poplar is generated by the insertion of an exogenous GS gene with the help of a binary vector.

In contrast, the present invention is drawn to a method of using "MS-like DNA fragments comprising a monotonous repeat of two to six nucleotides, wherein the DNA fragment has a length of about 70 to about 120 nucleotides long". In other words, the present invention is drawn to DNA repeating fragments having about 70 to about 120 nucleotides.

Applicants submit that the primary reference Havukkala et al. do not teach or suggest DNA repeating fragments having about 70 to about 120 nucleotides as claimed herein. Havukkala et al. only teach DNA repeating fragments that are way shorter than 70 nucleotides long (see Table 1, "repeat motif").

Hence, Applicants submit that neither the primary reference Havukkala et al., nor the combination of Havukkala and Gallardo, teach each and every aspect of the present invention, namely DNA repeating fragments having about 70 to

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about 120 nucleotides. Accordingly, Applicants respectfully request that the rejection of claims 60-61 and 63-68 under 35 U.S.C. 103(a) be withdrawn.

If a telephone interview would be of assistance in advancing prosecution of the present application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below. No fee is deemed necessary in connection with the filing of this Response. However, if a fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,

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